10/ 019,945

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NEWS	2		"Ask CAS" for self-help around the clock
NEWS	3	SEP 09	CA/CAplus records now contain indexing from 1907 to the present
NEWS	4	AUG 05	New pricing for EUROPATFULL and PCTFULL effective August 1, 2003
NEWS	5	AUG 13	Field Availability (/FA) field enhanced in BEILSTEIN
NEWS	6	AUG 18	Data available for download as a PDF in RDISCLOSURE
NEWS	7	AUG 18	Simultaneous left and right truncation added to PASCAL
NEWS	8	AUG 18	FROSTI and KOSMET enhanced with Simultaneous Left and Righ Truncation
NEWS	9	AUG 18	Simultaneous left and right truncation added to ANABSTR
NEWS	10	SEP 22	DIPPR file reloaded
NEWS	11	SEP 25	INPADOC: Legal Status data to be reloaded
NEWS	12	SEP 29	DISSABS now available on STN
NEWS	13	OCT 10	PCTFULL: Two new display fields added
NEWS	14	OCT 21	BIOSIS file reloaded and enhanced
NEWS	15	OCT 28	BIOSIS file segment of TOXCENTER reloaded and enhanced
NEWS	16	NOV 24	MSDS-CCOHS file reloaded

NEWS EXPRESS	NOVEMBER 14 CURRENT WINDOWS VERSION IS V6.01c, CURRENT MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP), AND CURRENT DISCOVER FILE IS DATED 23 SEPTEMBER 2003
NEWS HOURS	STN Operating Hours Plus Help Desk Availability
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NEWS PHONE	Direct Dial and Telecommunication Network Access to STN
NEWS WWW	CAS World Wide Web Site (general information)

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FILE 'HOME' ENTERED AT 09:16:26 ON 03 DEC 2003

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 09:16:37 ON 03 DEC 2003
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10/ 019,945

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 2 DEC 2003 HIGHEST RN 622845-74-3
DICTIONARY FILE UPDATES: 2 DEC 2003 HIGHEST RN 622845-74-3

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2003

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

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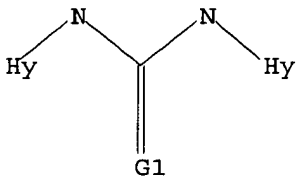
Uploading 10019945s.str

L1 STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1 STR



G1 O,S,N

Structure attributes must be viewed using STN Express query preparation.

=> s l1 ful
FULL SEARCH INITIATED 09:16:54 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - >1,000,000 TO ITERATE

< 35.6% PROCESSED 400000 ITERATIONS 53 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.43

FULL FILE PROJECTIONS: ONLINE **INCOMPLETE**
BATCH **INCOMPLETE**
PROJECTED ITERATIONS: EXCEEDS 1000000
PROJECTED ANSWERS: EXCEEDS 112

L2 53 SEA SSS FUL L1

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	148.55	148.76

FILE 'CAPLUS' ENTERED AT 09:17:46 ON 03 DEC 2003

10/ 019,945

FILE COVERS 1907 - 3 Dec 2003 VOL 139 ISS 23
FILE LAST UPDATED: 2 Dec 2003 (20031202/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l2
L3 13 L2

=> d l3 1- ibib abs hitstr
YOU HAVE REQUESTED DATA FROM 13 ANSWERS - CONTINUE? Y/(N):y

L3 ANSWER 1 OF 13 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:221654 CAPLUS
DOCUMENT NUMBER: 138:238029
TITLE: Preparation of ureas as vanilloid receptor (VR1) antagonists
INVENTOR(S): Rami, Harshad Kantilal; Thompson, Mervyn; Wyman, Paul Adrian
PATENT ASSIGNEE(S): Smithkline Beecham P.L.C., UK
SOURCE: PCT Int. Appl., 57 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

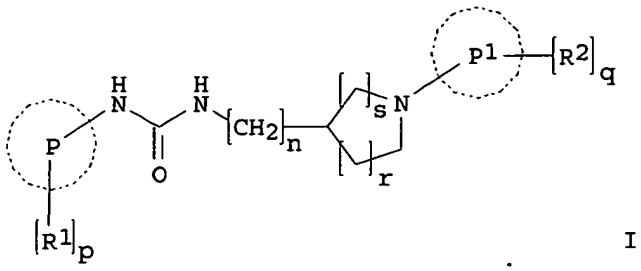
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003022809	A2	20030320	WO 2002-GB4206	20020913
WO 2003022809	A3	20030717		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

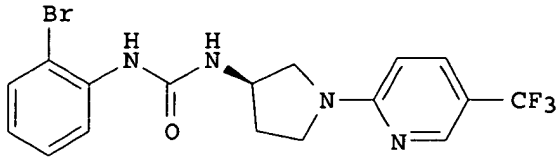
PRIORITY APPLN. INFO.: GB 2001-22156 A 20010913
GB 2001-30503 A 20011220
GB 2001-30505 A 20011220
GB 2001-30547 A 20011220
OTHER SOURCE(S): MARPAT 138:238029

10/ 019,945

GI



I



II

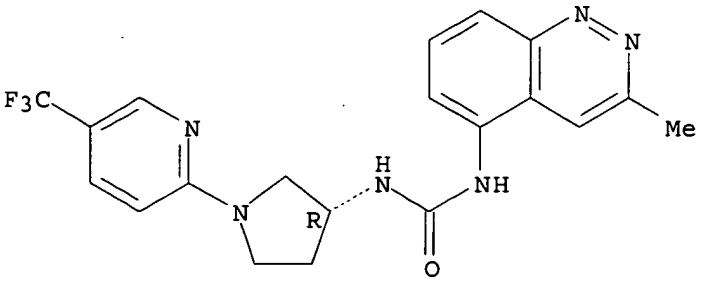
AB The title compds. [I; P, P1 = (hetero)aryl; R1, R2 = H, halo, alkyl, etc.; n = 0-3; p, q = 0-4; r = 1-3; s = 0-2], useful in medicine for the treatment and/or prophylaxis of pain, were prepd. Thus, reacting 2-bromophenyl isocyanate with (R)-1-(5-trifluoromethylpyridin-2-yl)-pyrrolidin-3-ylamine [claimed to be prepd. starting from 2-chloro-5-trifluoromethylpyridine and (3R)-3-(tert-butoxycarbonylamino)pyrrolidine; no data given] afforded (3R)-II. All compds., tested for vanilloid receptor (VR1) antagonist activity, had pKb > 6, preferred compds. having a pKb > 7.0.

IT **501952-15-4P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of ureas as vanilloid receptor (VR1) antagonists for treating pain)

RN 501952-15-4 CAPLUS

CN Urea, N-(3-methyl-5-cinnolinyl)-N'-[(3R)-1-[5-(trifluoromethyl)-2-pyridinyl]-3-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L3 ANSWER 2 OF 13 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:133246 CAPLUS
DOCUMENT NUMBER: 138:170245
TITLE: Preparation of aminophthalazinones as kinase

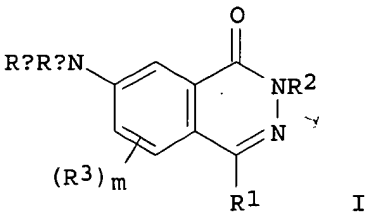
inhibitors.

INVENTOR(S): Pulici, Maurizio
PATENT ASSIGNEE(S): Pharmacia Italia S.P.A., Italy

SOURCE: PCT Int. Appl., 103 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003014090	A1	20030220	WO 2002-EP8544	20020730
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003073692	A1	20030417	US 2001-922729	20010807

PRIORITY APPLN. INFO.: US 2001-922729 A 20010807
OTHER SOURCE(S): MARPAT 138:170245
GI



I

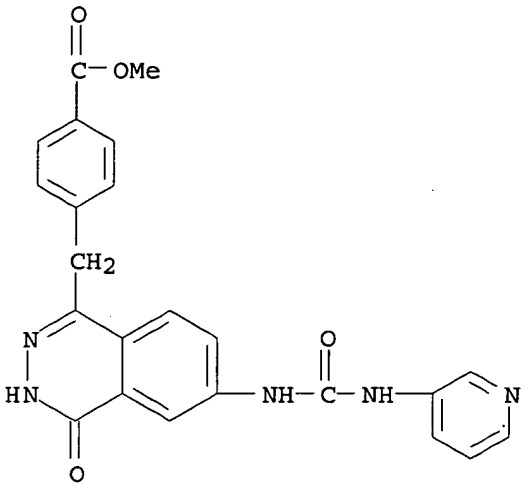
AB A method for treating diseases assocd. with altered protein kinase activity comprises administration of title compds. [I; Ra, Rb = H, (substituted) alkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocycloalkyl; or 1 or Ra, Rb = H, (substituted) alkyl, the other = COR', CONHR', CO2R', SO2R'; R' = H, (substituted) alkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl; R1 = CHR4R5; R4, R5 = H, (substituted) alkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl; or R1 = NHR', NR'COR'', NR'CONHR'', NR'SO2R''; R'' = H, R'; R2 = H, (substituted) alkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl; R3 = halo, NO2, CO2H, cyano, (substituted) alkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl; or R3 = COR', CONHR', SO2R', NR'R'', NR'COR'', NR'CONHR', NR'SO2R''; m = 0-3] (no data). Thus, 6-nitrophthalide was refluxed 11 h with Br2 and H2O2 in H2O to give 6-nitro-3-bromo-3H-isobenzofuran-1-one. The latter in Et propionate at 70-75.degree. was treated with PPh3 in Et propionate followed by heating and stirring overnight to give (5-amino-3-oxo-1,3-dihydroisobenzofuran-1-yl)triphenylphosphonium bromide. The latter in CH2Cl2/trifluoroethanol/HOAc was stirred 9 h with 4-(4-formyl-3-methoxyphenoxy)butyryl aminomethylated resin followed by addn. of BH3.pyridine to give after 40 h [5-[2-methoxy-4-[3-(4-resin-benzylcarbamoyl)propoxy]benzylamino]-3-oxo-1,3-dihydroisobenzofuran-1-

yl]triphenylphosphonium bromide. This was stirred with pyridine-3-carboxaldehyde and Et3N in CH2Cl2 for 20 h to give 4-[3-methoxy-4-[[3-oxo-1-(1-pyridin-3-ylmethylidene)-1,3-dihydroisobenzofuran-5-ylamino]methyl]phenoxy]-N-(4-resin-benzyl)butyramide. This was converted to N-(4-oxo-1-pyridin-3-ylmethyl-3,4-dihydrophthalazin-6-yl)benzamide. I are useful in the treatment of diseases caused by and/or assocd. with an altered protein kinase activity such as cancer, cell proliferative disorders, Alzheimer's disease, viral infections, autoimmune diseases and neurodegenerative disorders.

IT **497254-73-6P 497254-86-1P 497254-99-6P**
497255-12-6P 497255-25-1P 497255-38-6P
497255-51-3P 497255-64-8P 497255-77-3P
497255-91-1P 497256-04-9P 497256-17-4P
497256-33-4P 497256-53-8P 497256-66-3P
497256-79-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(claimed compd.; prepn. of aminophthalazinones as kinase inhibitors)

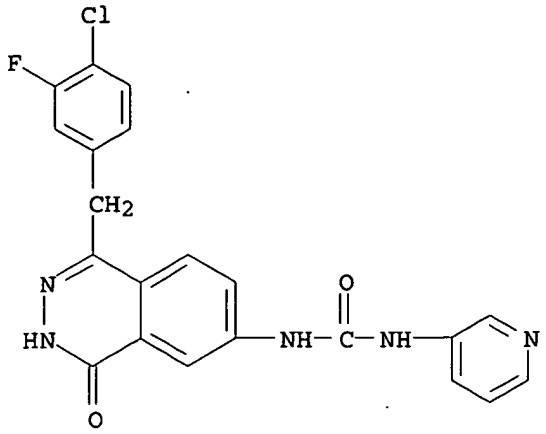
RN 497254-73-6 CAPLUS

CN Benzoic acid, 4-[[3,4-dihydro-4-oxo-6-[[(3-pyridinylamino)carbonyl]amino]-1-phthalazinyl]methyl]-, methyl ester (9CI) (CA INDEX NAME)



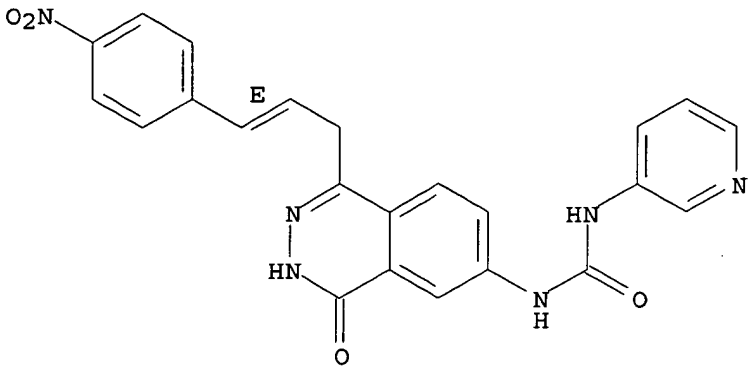
RN 497254-86-1 CAPLUS

CN Urea, N-[1-[(4-chloro-3-fluorophenyl)methyl]-3,4-dihydro-4-oxo-6-phthalazinyl]-N'-3-pyridinyl- (9CI) (CA INDEX NAME)

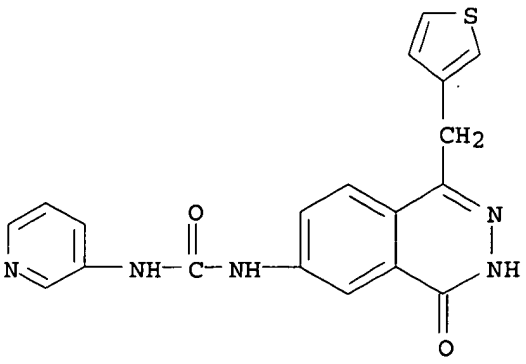


RN 497254-99-6 CAPLUS
CN Urea, N-[3,4-dihydro-1-[(2E)-3-(4-nitrophenyl)-2-propenyl]-4-oxo-6-phthalazinyl]-N'-3-pyridinyl- (9CI) (CA INDEX NAME)

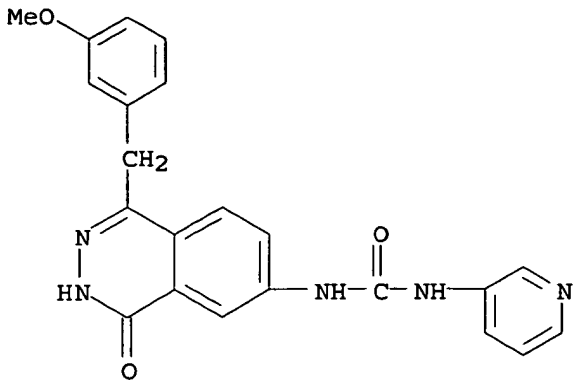
Double bond geometry as shown.



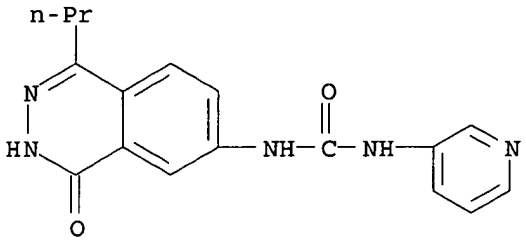
RN 497255-12-6 CAPLUS
CN Urea, N-[3,4-dihydro-4-oxo-1-(3-thienylmethyl)-6-phthalazinyl]-N'-3-pyridinyl- (9CI) (CA INDEX NAME)



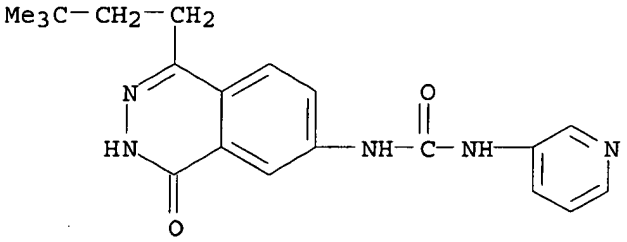
RN 497255-25-1 CAPLUS
CN Urea, N-[3,4-dihydro-1-[(3-methoxyphenyl)methyl]-4-oxo-6-phthalazinyl]-N'-3-pyridinyl- (9CI) (CA INDEX NAME)



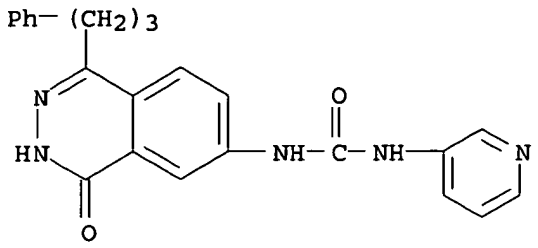
RN 497255-38-6 CAPLUS
CN Urea, N-(3,4-dihydro-4-oxo-1-propyl-6-phthalazinyl)-N'-3-pyridinyl- (9CI) (CA INDEX NAME)



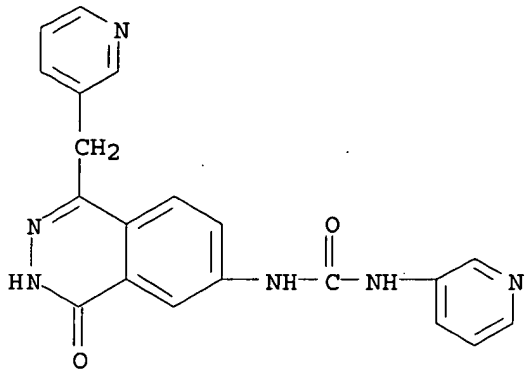
RN 497255-51-3 CAPLUS
CN Urea, N-[1-(3,3-dimethylbutyl)-3,4-dihydro-4-oxo-6-phthalazinyl]-N'-3-pyridinyl- (9CI) (CA INDEX NAME)



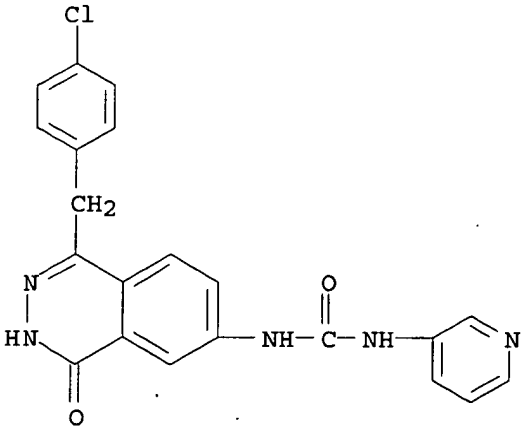
RN 497255-64-8 CAPLUS
CN Urea, N-[3,4-dihydro-4-oxo-1-(3-phenylpropyl)-6-phthalazinyl]-N'-3-pyridinyl- (9CI) (CA INDEX NAME)



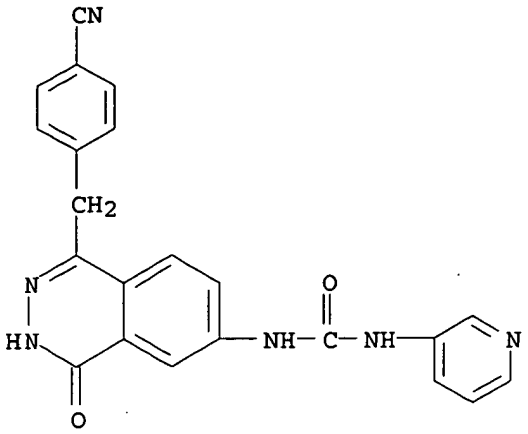
RN 497255-77-3 CAPLUS
CN Urea, N-[3,4-dihydro-4-oxo-1-(3-pyridinylmethyl)-6-phthalazinyl]-N'-3-pyridinyl- (9CI) (CA INDEX NAME)



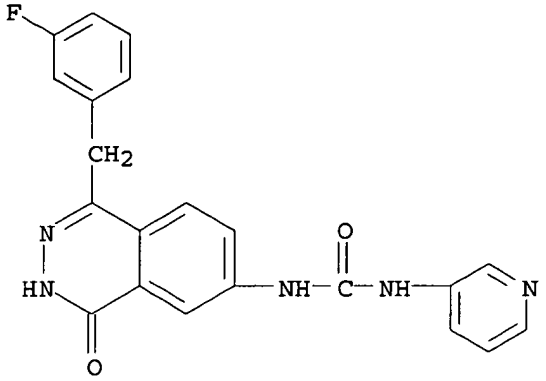
RN 497255-91-1 CAPLUS
CN Urea, N-[1-[(4-chlorophenyl)methyl]-3,4-dihydro-4-oxo-6-phthalazinyl]-N'-3-pyridinyl- (9CI) (CA INDEX NAME)



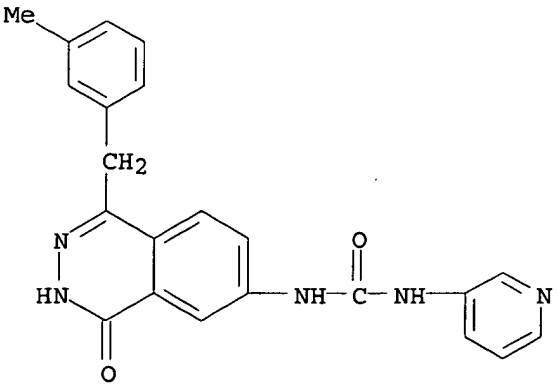
RN 497256-04-9 CAPLUS
CN Urea, N-[1-[(4-cyanophenyl)methyl]-3,4-dihydro-4-oxo-6-phthalazinyl]-N'-3-pyridinyl- (9CI) (CA INDEX NAME)



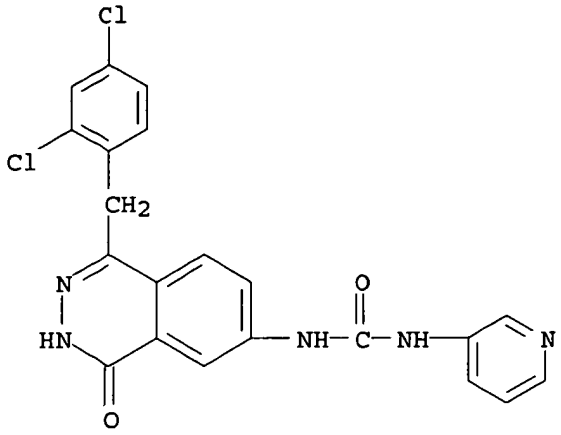
RN 497256-17-4 CAPLUS
CN Urea, N-[1-[(3-fluorophenyl)methyl]-3,4-dihydro-4-oxo-6-phthalazinyl]-N'-3-pyridinyl- (9CI) (CA INDEX NAME)



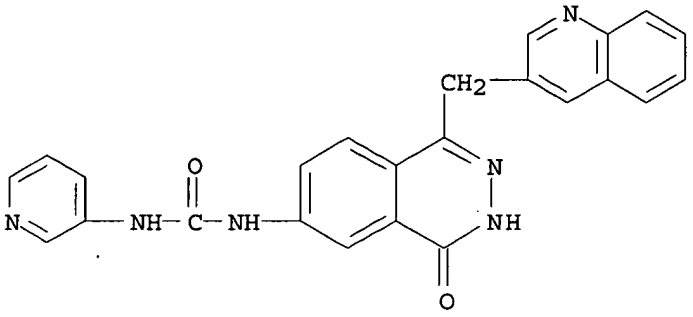
RN 497256-33-4 CAPLUS
CN Urea, N-[3,4-dihydro-1-[(3-methylphenyl)methyl]-4-oxo-6-phthalazinyl]-N'-3-pyridinyl- (9CI) (CA INDEX NAME)



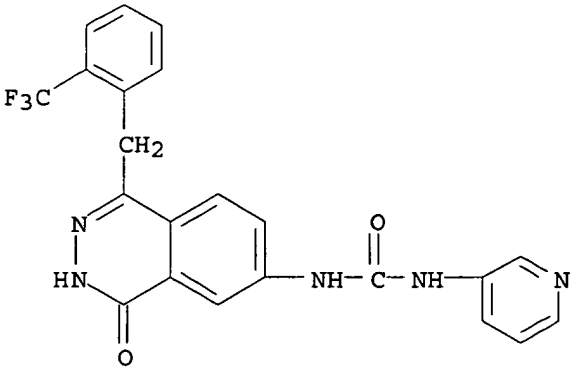
RN 497256-53-8 CAPLUS
CN Urea, N-[1-[(2,4-dichlorophenyl)methyl]-3,4-dihydro-4-oxo-6-phthalazinyl]-N'-3-pyridinyl- (9CI) (CA INDEX NAME)



RN 497256-66-3 CAPLUS
CN Urea, N-[3,4-dihydro-4-oxo-1-(3-quinolinylmethyl)-6-phthalazinyl]-N'-3-pyridinyl- (9CI) (CA INDEX NAME)



RN 497256-79-8 CAPLUS
CN Urea, N-[3,4-dihydro-4-oxo-1-[[2-(trifluoromethyl)phenyl]methyl]-6-phthalazinyl]-N'-3-pyridinyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 3 OF 13 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:965133 CAPLUS
DOCUMENT NUMBER: 138:39277

10/ 019,945

TITLE: Preparation of N-thiazolyl-N'-pyridyl ureas as antitumor agents

INVENTOR(S): Askew, Benny C.; De Morin, Frenel F.; Hague, Andrew; Laber, Ellen; Li, Aiwen; Liu, Gang; Lopez, Patricia; Nomak, Rana; Santora, Vincent; Tegley, Christopher; Yang, Kevin

PATENT ASSIGNEE(S): Amgen, Inc., USA

SOURCE: U.S. Pat. Appl. Publ., 129 pp., Cont.-in-part of U. S. Ser. No. 930,753.
CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002193405	A1	20021219	US 2002-77124	20020215
US 6645990	B2	20031111		
US 2002173507	A1	20021121	US 2001-930753	20010814
WO 2003070727	A1	20030828	WO 2003-US4537	20030213

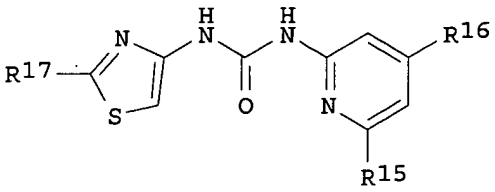
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:
US 2000-225793P P 20000815
US 2001-930753 A2 20010814
US 2002-77124 A 20020215

OTHER SOURCE(S): MARPAT 138:39277

GI



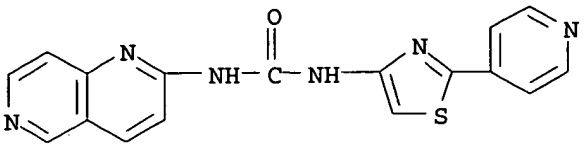
I

AB The title compds. [I; R15 = H, heterocyclyl, Ph, etc.; R16 = H, heterocyclylcarbonyl, alkylaminocarbonyl, etc.; R17 = halo, alkyl, cycloalkyl, etc.; provided only one of R15 and R16 = H] which are effective for prophylaxis and treatment of diseases, such as cell proliferation or apoptosis mediated diseases involving stroke, cancer and the like, were prepd. Thus, heating 2-phenyl-4-thiazolylcarbonylazide with 6-(3-methylpiperidin-1-ylmethyl)pyridin-2-ylamine in PhMe afforded the urea I [R15 = 3-methylpiperidin-1-ylmethyl; R16 = H; R17 = Ph] which showed cdk2/cyclin and cdk5/p25 kinase activity with IC50 of < 0.5 .mu.M.

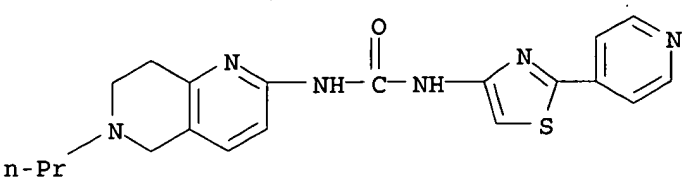
IT **400774-22-3P 400774-24-5P 400774-25-6P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of N-thiazolyl-N'-pyridyl ureas as antitumor agents)

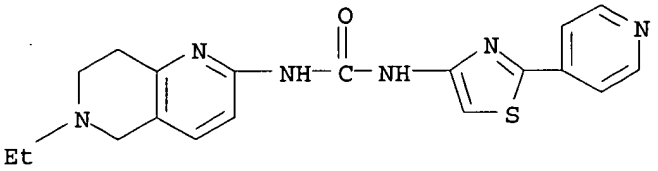
RN 400774-22-3 CAPLUS
CN Urea, N-1,6-naphthyridin-2-yl-N'-[2-(4-pyridinyl)-4-thiazolyl]- (9CI) (CA INDEX NAME)



RN 400774-24-5 CAPLUS
CN Urea, N-[2-(4-pyridinyl)-4-thiazolyl]-N'-(5,6,7,8-tetrahydro-6-propyl-1,6-naphthyridin-2-yl)- (9CI) (CA INDEX NAME)



RN 400774-25-6 CAPLUS
CN Urea, N-(6-ethyl-5,6,7,8-tetrahydro-1,6-naphthyridin-2-yl)-N'-[2-(4-pyridinyl)-4-thiazolyl]- (9CI) (CA INDEX NAME)

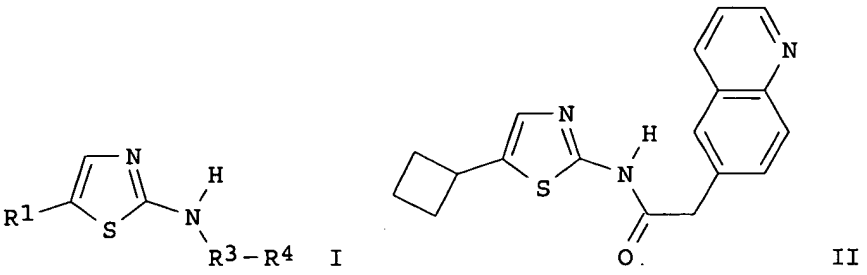


L3 ANSWER 4 OF 13 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:866687 CAPLUS
DOCUMENT NUMBER: 137:353013
TITLE: Thiazole derivatives and their use as cdk inhibitors, including combinations and pharmaceutical compositions
INVENTOR(S): Cooper, Christopher Blair; Helal, Christopher John; Sanner, Mark Allen
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: Eur. Pat. Appl., 32 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1256578	A1	20021113	EP 2002-253106	20020502
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2002338556	A2	20021127	JP 2002-132275	20020508
BR 2002001691	A	20030311	BR 2002-1691	20020513
US 2003078252	A1	20030424	US 2002-144403	20020513

10/ 019,945

PRIORITY APPLN. INFO.: US 2001-290466P P 20010511
OTHER SOURCE(S): MARPAT 137:353013
GI



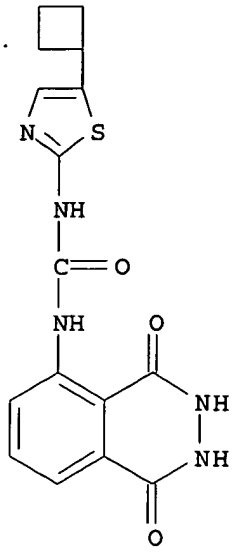
I II

AB The invention provides compds. thiazole derivs. I [wherein: R1 = (un)substituted alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, heterocycloalkyl, bicycloalkyl, bicycloalkenyl, heterobicycloalkyl, aryl, heteroaryl, or amino including cyclic amino; R3 = (un)substituted CONH, COO, CO(CH2)n, (CH2)n; R4 = as given for R1 except amino; n = 0-3; including pharmaceutically acceptable salts]. I are inhibitors of cyclin-dependent protein kinases (cdk), particularly cdk5, cdk2, and GSK-3. Pharmaceutical compns. and methods comprising compds. I are described, particularly for treating diseases and conditions comprising abnormal cell growth, such as cancer, and neurodegenerative diseases and conditions and those affected by dopamine neurotransmission. Also described are pharmaceutical compns. and methods comprising compds. I for treating or improving the following: male fertility and sperm motility problems, diabetes mellitus, impaired glucose tolerance, metabolic syndrome or syndrome X, polycystic ovary syndrome, adipogenesis and obesity, myogenesis and frailty (for example age-related decline in phys. performance), acute sarcopenia (for example, muscle atrophy and/or cachexia assocd. with burns, bed rest, limb immobilization, or major thoracic, abdominal, and/or orthopedic surgery), sepsis, hair loss, hair thinning, balding, and immunodeficiency. Approx. 90 specific compds. I are claimed, and the prepns. of 5 of these and several intermediates are exemplified. For instance, 2-aminothiazole was lithiated and silylated, then re-lithiated and treated with cyclobutanone to give 1-(2-aminothiazol-5-yl)cyclobutanol. This alc. was hydrogenated to give 5-cyclobutylthiazol-2-ylamine, which was coupled with 6-quinolylacetic acid using T3P (1-propanephosphonic acid cyclic trimeric anhydride), to give title compd. II. The 5 exemplified compds. all had IC50 values of < 50 .mu.M for inhibiting cdk5, cdk2, and GSK-3.beta. in vitro.

IT **474460-95-2P**, 1-(5-Cyclobutylthiazol-2-yl)-3-(1,4-dioxo-1,2,3,4-tetrahydrophthalazin-5-yl)urea
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; prepn. of thiazole derivs. as cdk inhibitors)

RN 474460-95-2 CAPLUS

CN Urea, N-(5-cyclobutyl-2-thiazolyl)-N'-(1,2,3,4-tetrahydro-1,4-dioxo-5-phthalazinyl)- (9CI) (CA INDEX NAME)



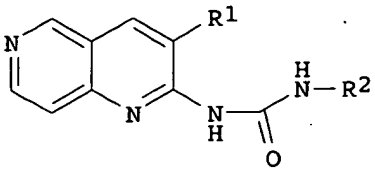
REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 5 OF 13 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:594630 CAPLUS
DOCUMENT NUMBER: 137:150266
TITLE: Naphthyridine compounds for treatment of mammalian diseases
INVENTOR(S): Semones, Marcus A.
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002060382	A2	20020808	WO 2002-US1474	20020118
WO 2002060382	A3	20020926		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-262862P P 20010119
OTHER SOURCE(S): MARPAT 137:150266
GI



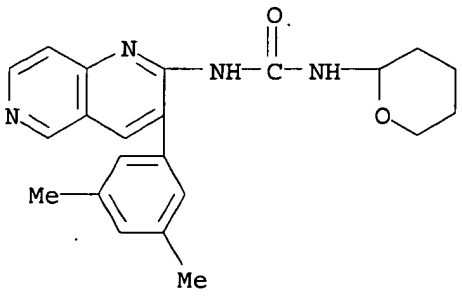
I

AB The present invention relates to naphthyridine compds. (I: R1 = aryl, aralkyl, heteroaryl, heteroarylalkyl, heterocyclic, heterocyclic alkyl, aroyl, alkanoyl; R2 = H, C1-10 alkyl, cycloalkyl, aryl, aralkyl, heteroaryl, heteroaryl alkyl, heterocyclic, heterocyclic alkyl, alkenyl, cycloalkenyl, alkynyl; R1 and R2 may be independently optionally substituted) and the treatment of mammalian diseases in which inappropriate, excessive or undesirable angiogenesis has occurred and/or where excessive Tie2 receptor kinase activity has occurred. Naphthyridine compds. have IC50 in the range of 1-104 nM, typically in the 700-104 nM range. For example, 3-(2,6-dichlorophenyl)-1,6-naphthyridin-2'-2-[N'-(1,1-dimethylethyl)urea] was prepd. in a yield of 36% (25 mg) by the reaction of 100 mg of 4-aminonicotinaldehyde and 217 mg of 2,6-dichlorophenylacetonitrile to obtain 191 mg of 3-(2,6-dichlorophenyl)-1,6-naphthyridin-2-amine, followed by the reaction of 51 mg of 3-(2,6-dichlorophenyl)-1,6-naphthyridin-2-amine obtained with 17 mg of tert-Bu isocyanate. A model of inflammatory angiogenesis are used to show that inhibition of Tie2 will stop the tissue destruction of excessive, inappropriate or undesirable proliferation of blood vessels.

IT **444880-63-1P 444880-64-2P 444880-65-3P**
444880-66-4P 444880-67-5P 444880-68-6P
444880-69-7P 444880-70-0P 444880-71-1P
444880-72-2P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(naphthyridine compds. for treatment of mammalian diseases characterized with undesirable angiogenesis)

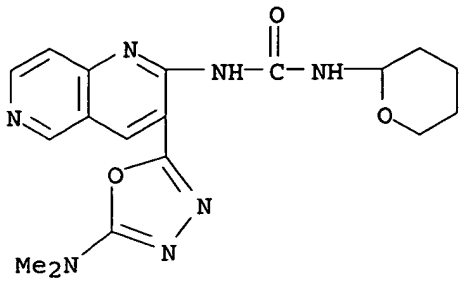
RN 444880-63-1 CAPLUS

CN Urea, N-[3-(3,5-dimethylphenyl)-1,6-naphthyridin-2-yl]-N'-(tetrahydro-2H-pyran-2-yl)- (9CI) (CA INDEX NAME)

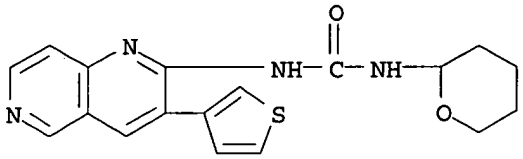


RN 444880-64-2 CAPLUS

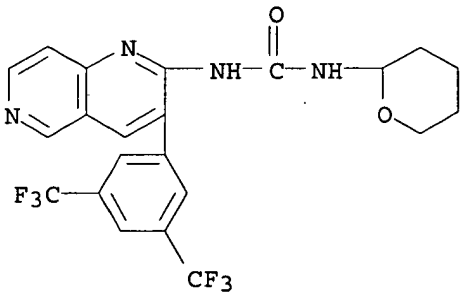
CN Urea, N-[3-[5-(dimethylamino)-1,3,4-oxadiazol-2-yl]-1,6-naphthyridin-2-yl]-N'-(tetrahydro-2H-pyran-2-yl)- (9CI) (CA INDEX NAME)



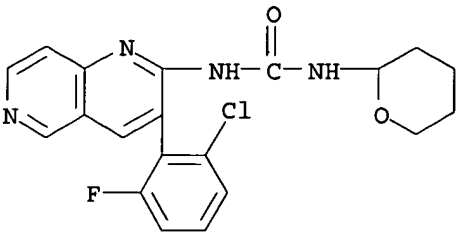
RN 444880-65-3 CAPLUS
CN Urea, N-(tetrahydro-2H-pyran-2-yl)-N'-[3-(3-thienyl)-1,6-naphthyridin-2-yl]- (9CI) (CA INDEX NAME)



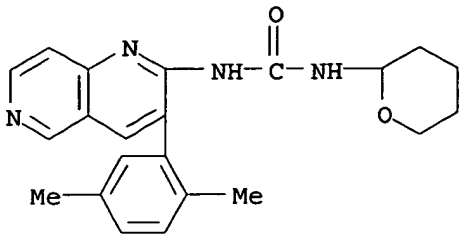
RN 444880-66-4 CAPLUS
CN Urea, N-[3-[3,5-bis(trifluoromethyl)phenyl]-1,6-naphthyridin-2-yl]-N'-(tetrahydro-2H-pyran-2-yl)- (9CI) (CA INDEX NAME)



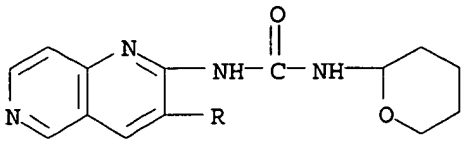
RN 444880-67-5 CAPLUS
CN Urea, N-[3-(2-chloro-6-fluorophenyl)-1,6-naphthyridin-2-yl]-N'-(tetrahydro-2H-pyran-2-yl)- (9CI) (CA INDEX NAME)

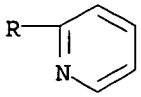


RN 444880-68-6 CAPLUS
CN Urea, N-[3-(2,5-dimethylphenyl)-1,6-naphthyridin-2-yl]-N'-(tetrahydro-2H-pyran-2-yl)- (9CI) (CA INDEX NAME)

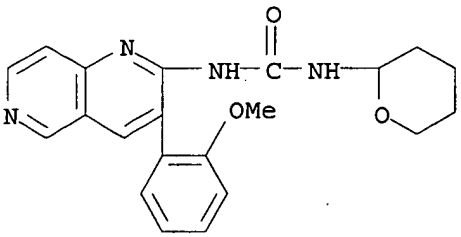


RN 444880-69-7 CAPLUS
CN Urea, N-[3-(2-pyridinyl)-1,6-naphthyridin-2-yl]-N'-(tetrahydro-2H-pyran-2-yl)- (9CI) (CA INDEX NAME)

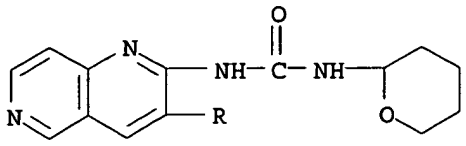


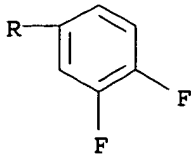


RN 444880-70-0 CAPLUS
CN Urea, N-[3-(2-methoxyphenyl)-1,6-naphthyridin-2-yl]-N'-(tetrahydro-2H-pyran-2-yl)- (9CI) (CA INDEX NAME)

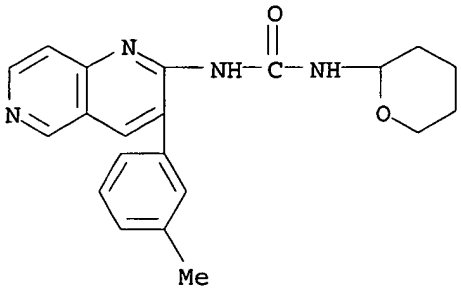


RN 444880-71-1 CAPLUS
CN Urea, N-[3-(3,4-difluorophenyl)-1,6-naphthyridin-2-yl]-N'-(tetrahydro-2H-pyran-2-yl)- (9CI) (CA INDEX NAME)





RN 444880-72-2 CAPLUS
CN Urea, N-[3-(3-methylphenyl)-1,6-naphthyridin-2-yl]-N'-(tetrahydro-2H-pyran-2-yl)- (9CI) (CA INDEX NAME)



L3 ANSWER 6 OF 13 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:591913 CAPLUS
DOCUMENT NUMBER: 137:150215
TITLE: Cdk4 and/or Cdk6 inhibitors with biaryl ureas and their salts as antitumor agents
INVENTOR(S): Hatayama, Satoshi; Hayashi, Kyoko; Honma, Mitsuki; Takahashi, Ikuko
PATENT ASSIGNEE(S): Banyu Pharmaceutical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 194 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2002220338	A2	20020809	JP 2001-18755	20010126

PRIORITY APPLN. INFO.: JP 2001-18755 20010126
OTHER SOURCE(S): MARPAT 137:150215
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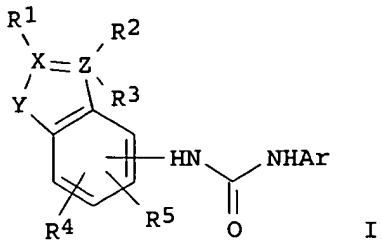


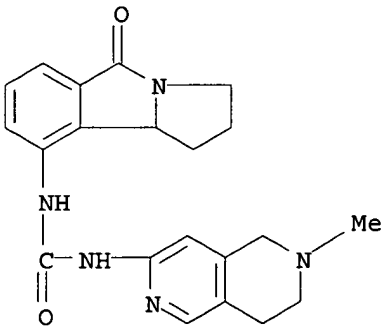
I

AB This invention relates to the general structures (I; Ar = N-contg. hetero arom. ring, X, Z = C, etc.; Y = CO, etc.; R1-R5 = H, etc.) and their salts as Cdk4 and/or Cdk6 inhibitors. I have antiproliferative effects on cancer cells and are potential antitumor agents. Formulation examples of I capsules, tablets, and injections were given.

IT **322686-07-7 322686-08-8 322686-09-9**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Cdk4 and/or Cdk6 inhibitors with biaryl ureas and their salts as antitumor agents)

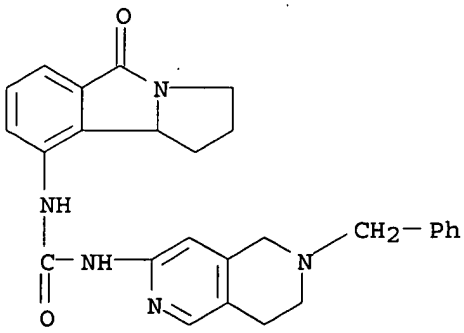
RN 322686-07-7 CAPLUS

CN Urea, N-(5,6,7,8-tetrahydro-6-methyl-2,6-naphthyridin-3-yl)-N'-(2,3,5,9b-tetrahydro-5-oxo-1H-pyrrolo[2,1-a]isoindol-9-yl)- (9CI) (CA INDEX NAME)



RN 322686-08-8 CAPLUS

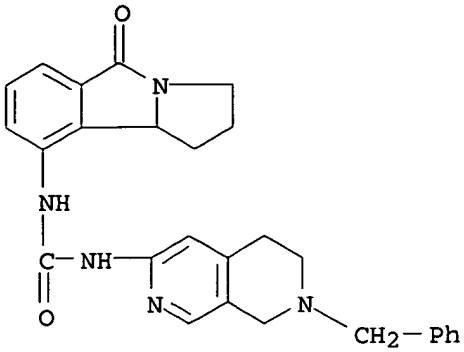
CN Urea, N-(2,3,5,9b-tetrahydro-5-oxo-1H-pyrrolo[2,1-a]isoindol-9-yl)-N'-[5,6,7,8-tetrahydro-6-(phenylmethyl)-2,6-naphthyridin-3-yl]- (9CI) (CA INDEX NAME)



RN 322686-09-9 CAPLUS

10/ 019,945

CN Urea, N-(2,3,5,9b-tetrahydro-5-oxo-1H-pyrrolo[2,1-a]isoindol-9-yl)-N'-[5,6,7,8-tetrahydro-7-(phenylmethyl)-2,7-naphthyridin-3-yl]- (9CI) (CA INDEX NAME)



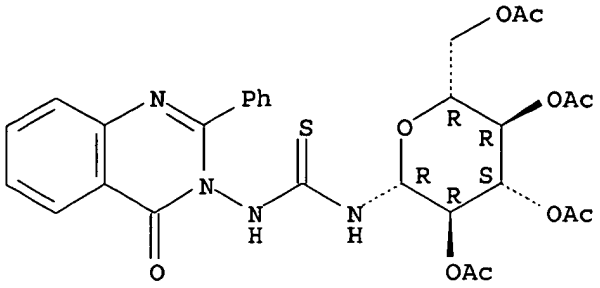
L3 ANSWER 7 OF 13 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:323136 CAPLUS
DOCUMENT NUMBER: 137:93926
TITLE: Synthesis and Antiviral Evaluation of Some New Glycosylthioureas Containing a Quinazolinone Nucleus
AUTHOR(S): Saleh, Mohamed A.; Abdel-Megged, Mohamed F.; Abdo, Mohamed A.; Shokr, Abdel-Basset M.
CORPORATE SOURCE: Chemistry Department, Faculty of Science, Tanta University, Tanta, Egypt
SOURCE: Nucleosides, Nucleotides & Nucleic Acids (2002), 21(1), 93-106
CODEN: NNNAFY; ISSN: 1525-7770
PUBLISHER: Marcel Dekker, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 137:93926

AB A new synthesis of glycosylthioureas contg. a quinazolinone nucleus is described utilizing per-O-acetylglycopyranosylisothiocyanates and several aminoquinazolinones as starting compds. Structural proofs of these compds. are provided from elemental analyses, IR, 1H and 13C NMR spectra and mass spectra. The biol. activity of these compds. has been studied and show no activity against Human Immunodeficiency Virus (HIV) or against various tumor viruses.

IT **442637-38-9P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(synthesis, anti-HIV, and antitumor evaluation of some new glycosylthioureas contg. a quinazolinone nucleus)

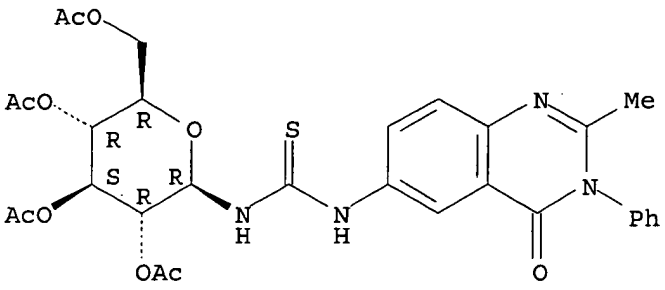
RN 442637-38-9 CAPLUS
CN Thiourea, N-(4-oxo-2-phenyl-3(4H)-quinazolinyl)-N'-(2,3,4,6-tetra-O-acetyl-.beta.-D-glucopyranosyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



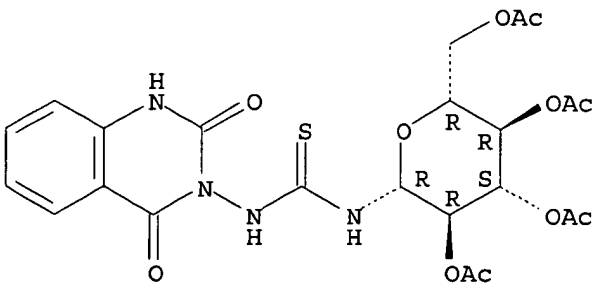
IT **442637-33-4P 442637-43-6P 442637-54-9P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis, anti-HIV, and antitumor evaluation of some new glycosylthioureas contg. a quinazolinone nucleus)
RN 442637-33-4 CAPLUS
CN Thiourea, N-(3,4-dihydro-2-methyl-4-oxo-3-phenyl-6-quinazolinyl)-N'-(2,3,4,6-tetra-O-acetyl-.beta.-D-glucopyranosyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



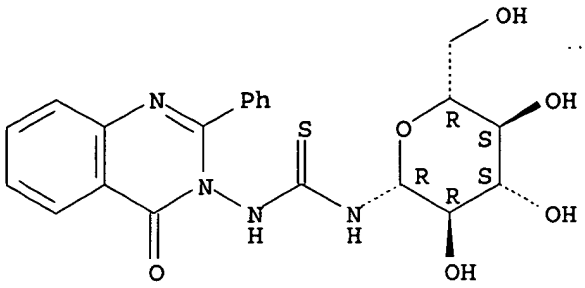
RN 442637-43-6 CAPLUS
CN Thiourea, N-(1,4-dihydro-2,4-dioxo-3(2H)-quinazolinyl)-N'-(2,3,4,6-tetra-O-acetyl-.beta.-D-glucopyranosyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 442637-54-9 CAPLUS
CN Thiourea, N-.beta.-D-glucopyranosyl-N'-(4-oxo-2-phenyl-3(4H)-quinazolinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

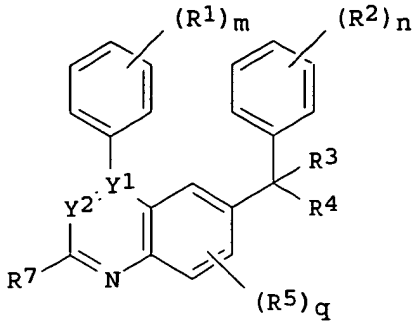


REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 8 OF 13 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:240759 CAPLUS
DOCUMENT NUMBER: 136:279469
TITLE: Preparation of quinoline and quinazoline derivatives as farnesyl transferase inhibitors for treatment of tumors and proliferative diseases
INVENTOR(S): Angibaud, Patrick Rene; Venet, Marc Gaston; Pilatte, Isabelle Noeelle Constance
PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.
SOURCE: PCT Int. Appl., 66 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002024682	A1	20020328	WO 2001-EP10867	20010918
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1322635	A1	20030702	EP 2001-974271	20010918
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
AU 2001093826	A5	20020402	AU 2001-93826	20020402
US 2003203904	A1	20031030	US 2003-381363	20030324

PRIORITY APPLN. INFO.: EP 2000-203365 A 20000925
WO 2001-EP10867 W 20010918
OTHER SOURCE(S): MARPAT 136:279469
GI



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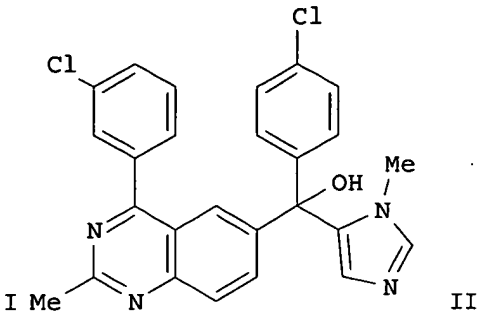


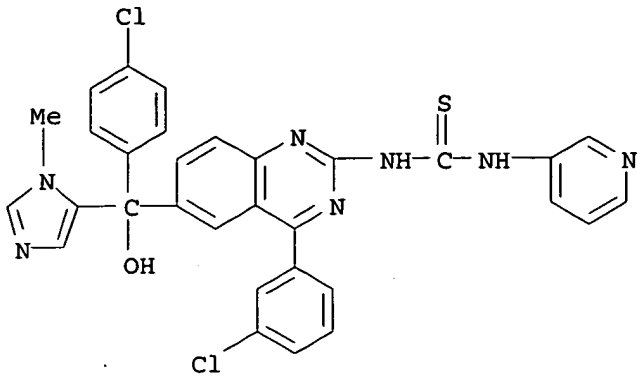
II

AB Title compds. I [wherein m and n = independently 0-5; q = 0-3; Y1Y2 = C:N or C:CR9; C9 = H, halo, CN, (cyclo)alkyl, hydroxyalkyl, alkoxy(alkyl), aminoalkyl, (amino)alkenyl, (amino)alkynyl, halocarbonyl, hydroxycarbonyl, alkoxycarbonyl, aryl, (un)substituted amino or carbamoyl, etc.; R1 and R2= independently azido, OH, halo, CN, NO2, trihalomethyl, alkoxy, aryloxy, heterocyclyloxy, alkylthio, or (un)substituted (cyclo)alkyl, alkenyl, alkynyl, carbamoyl, amino, sulfamoyl, etc.; or R1R2 = OCH2O, OCH2CH2O, OCH:CH, OCH2CH2, OCH2CH2CH2, CH:CHCH:CH; R3 = H, halo, CN, alkenyl, alkynyl, hydroxycarbonyl, alkoxycarbonyl, aryl, heterocyclyl, alkoxy, alkylthio, (un)substituted (cyclo)alkyl or amino, etc.; R4 = (un)substituted imidazolyl, triazolyl, or pyridyl; R5 = CN, OH, halo, alkenyl, alkynyl, hydroxycarbonyl, alkoxycarbonyl, or (un)substituted (cyclo)alkyl, alkoxy, amino, or carbamoyl, etc.; R7 = halo or (un)substituted (cyclo)alkyl, alkenyl, alkynyl, alkylthio, carboxy, carbamoyl, acyl(amino), etc.; or pharmaceutically acceptable salts, N-oxides, or stereochem. isomeric forms thereof] were prepd. For example, N-[2-(3-chlorobenzoyl)-4-(4-chlorobenzoyl)phenyl]acetamide was cyclized with NH3 in i-PrOH to give (4-chlorophenyl)[4-(3-chlorophenyl)-2-methyl-6-quinazolinyl]methanone (36%). Addn. of 1-methyl-1H-imidazole in the presence of BuLi and SiEt3Cl in THF afforded II (40%). I have potent farnesyl transferase inhibitory effect and are useful for inhibiting proliferative diseases and growth of tumors expressing an activated ras oncogene (no data).

IT **405550-33-6P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(farnesyl transferase inhibitor; prepn. of quinoline and quinazoline derivs. as farnesyl transferase inhibitors for treatment of tumors and proliferative diseases)

RN 405550-33-6 CAPLUS

CN Thiourea, N-[4-(3-chlorophenyl)-6-[(4-chlorophenyl)hydroxy(1-methyl-1H-imidazol-5-yl)methyl]-2-quinazolinyl]-N'-3-pyridinyl- (9CI) (CA INDEX NAME)

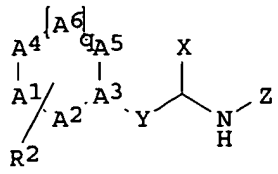


REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 9 OF 13 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:142704 CAPLUS
DOCUMENT NUMBER: 136:200177
TITLE: Preparation of diheteroaryl ureas as antitumor agents
INVENTOR(S): Santora, Vent; Askew, Benny; Ghose, Arup; Hague, Andrew; Kim, Tae Seong; Laber, Ellen; Li, Aiwen; Lian, Brian; Liu, Gang; Norman, Mark Henry; Smith, Leon; Tasker, Andrew; Tegley, Christopher; Yang, Kevin
PATENT ASSIGNEE(S): Amgen Inc., USA
SOURCE: PCT Int. Appl., 371 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002014311	A2	20020221	WO 2001-US25472	20010815
WO 2002014311	A3	20020919		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2001084909	A5	20020225	AU 2001-84909	20010815
EP 1309589	A2	20030514	EP 2001-964009	20010815
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.: US 2000-225793P P 20000815
WO 2001-US25472 W 20010815
OTHER SOURCE(S): MARPAT 136:200177
GI



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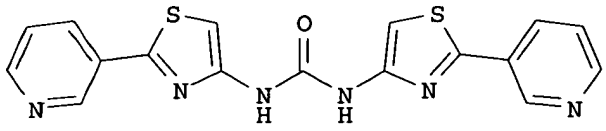


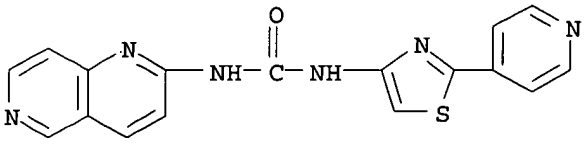
II

AB The title compds. [I; A1-A6 = CH2, CH, C, O, S, Nh, N; X and Z taken together to form a N atom contg. ring; Y = NHCO(CH2)p, CH2CO2, NHSO2CH2, NHCO2, NHCONR6(CH2)r; R2 = alkylaminoalkynyl, cycloalkenylalkynyl, phenylalkynyl, etc.; p = 1-2; q = 0-1; r = 0-3; R6 is not defined] which are effective for prophylaxis and treatment of diseases, such as cell proliferation or apoptosis mediated diseases involving stroke, cancer and the like, were prepd. Thus, treating 3-(3-pyridyl)-4-thiazolylcarbonylazide in PhMe with a few drops of H2O afforded the urea II which showed cdk2/cyclin and cdk5/cyclin kinase activity with IC50 of < 50 .mu.M.

IT **400774-22-3P 400774-24-5P 400774-25-6P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of diheteroaryl ureas as antitumor agents)

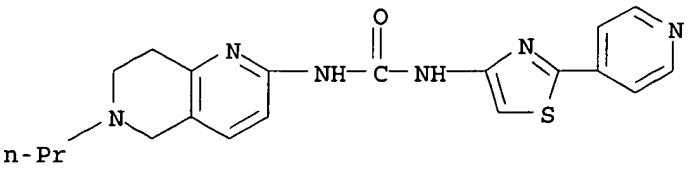
RN 400774-22-3 CAPLUS

CN Urea, N-1,6-naphthyridin-2-yl-N'-[2-(4-pyridinyl)-4-thiazolyl]- (9CI) (CA INDEX NAME)



RN 400774-24-5 CAPLUS

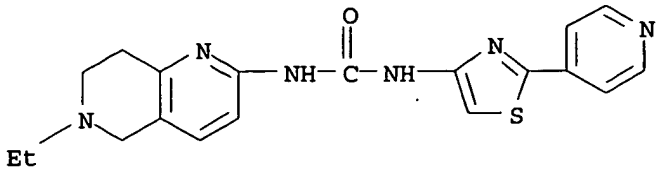
CN Urea, N-[2-(4-pyridinyl)-4-thiazolyl]-N'-(5,6,7,8-tetrahydro-6-propyl-1,6-naphthyridin-2-yl)- (9CI) (CA INDEX NAME)



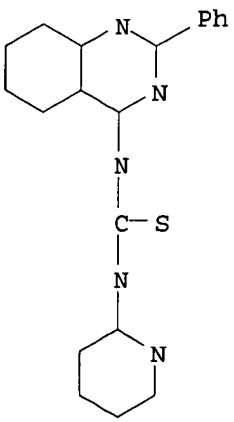
RN 400774-25-6 CAPLUS

CN Urea, N-(6-ethyl-5,6,7,8-tetrahydro-1,6-naphthyridin-2-yl)-N'-[2-(4-pyridinyl)-4-thiazolyl]- (9CI) (CA INDEX NAME)

10/ 019,945



L3 ANSWER 10 OF 13 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:727667 CAPLUS
DOCUMENT NUMBER: 136:183778
TITLE: One-pot quinazolin-4-ylthiourea synthesis via N-(2-cyanophenyl)benzimidoyl isothiocyanate
AUTHOR(S): Fathalla, W.; Cajan, M.; Marek, J.; Pazdera, P.
CORPORATE SOURCE: Dep. Org. Chem., Faculty Science, Masaryk Univ., Brno, Czech Rep.
SOURCE: Molecules [online computer file] (2001), 6(7), 588-602
CODEN: MOLEFW; ISSN: 1420-3049
URL: http://www.mdpi.org/molecules/papers/60700588.pdf
PUBLISHER: Molecular Diversity Preservation International
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB 1-Substituted-3-(2-phenylquinazolin-4-yl) thioureas were produced by an intramol. cycloaddn. reaction of 1-substituted-3-[(2-cyanophenylimino)phenylmethyl] thioureas. These compds. in turn were prepd. by the reaction of N-(2-cyanophenyl)benzimidoyl isothiocyanate with primary amines. The structures were confirmed by FTIR, 1H-NMR, 13C-NMR, mass spectroscopy and x-ray crystallog.
IT **400053-16-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of (phenylquinazolinyl) thioureas by intramol. cycloaddn. reaction of [(cyanophenylimino)phenylmethyl] thioureas)
RN 400053-16-9 CAPLUS
CN Thiourea, N-(2-phenyl-4-quinazolinyl)-N'-2-pyridinyl- (9CI) (CA INDEX NAME)



*** FRAGMENT DIAGRAM IS INCOMPLETE ***
REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 11 OF 13 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:719183 CAPLUS
DOCUMENT NUMBER: 136:37266
TITLE: Complexation-Induced Unfolding of Heterocyclic Ureas.

10/ 019,945

Simple Foldamers Equilibrate with Multiply Hydrogen-Bonded Sheetlike Structures

AUTHOR(S): Corbin, Perry S.; Zimmerman, Steven C.; Thiessen, Paul A.; Hawryluk, Natalie A.; Murray, Thomas J.

CORPORATE SOURCE: Department of Chemistry, University of Illinois, Urbana, IL, 61801, USA

SOURCE: Journal of the American Chemical Society (2001), 123(43), 10475-10488
CODEN: JACSAT; ISSN: 0002-7863

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The synthesis and conformational studies of heterocyclic ureas (amides) N,N'-Di-2-pyridylurea (I), 2,7-Dipentanoylamido-1,8-naphthyridine (II), N-Butyl-N'-(1,8-naphthyridin-2-yl)urea (III), N-Butyl-N'-(4-methylpyridin-2-yl)urea (IV), 2-Pentanoylamido-1,8-naphthyridine (V), Bis-2,7-(3-(3,4,5-tridodecyloxyphenyl)uryl)-1,8-naphthyridine (VI), and N,N'-Di-((5,7-dipropyl-(1,8-naphthyridin))-2-yl)urea (VII) and their concn.-dependent unfolding to form multiply hydrogen-bonded complexes are described. Ureas I and VII were prepd. by reacting 2-aminopyridine and aminonaphthyridine , resp., with triphosgene and 4-(dimethylamino)pyridine (DMAP). Heterocyclic ureas III and IV, were prepd. by treating their corresponding amino precursors with butylisocyanate, whereas bisureido naphthyridines VI was prepd. by heating 2,7-diamino-1,8-naphthyridine (13) with butylisocyanate and 3,4,5-tridodecyloxyphenyl isocyanate, resp. The hydrogen-bonding modules II and V were synthesized. X-ray crystallog. analyses were performed on ureas I and III, , indicating that these ureas are intramolecularly hydrogen-bonded in the solid state. Moreover, detailed 1H NMR soln. studies of indicate that similar folded structures form in chloroform. In addn., naphthyridinylureas III and VII unfold and dimerize by forming four hydrogen bonds at high concns., and ureas I and IV unfold in the presence of their hydrogen-bonding complements, amides II and V, to form complexes with three and four hydrogen bonds, resp. Likewise, the mixing of VI and VII results in a mutual unfolding and formation of a robust, sheetlike, sextuply hydrogen-bonded complex. The hydrogen-bonding modules described are useful building blocks for self-assembly, and the unfolding process represents a very primitive mimicry of the helix-to-sheet transition shown by peptides and potentially shown by the hypothetical naphthyridinylurea .

IT **380441-61-2**
RL: FMU (Formation, unclassified); PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); FORM (Formation, nonpreparative); PROC (Process)
(crystallog. and NMR spectroscopy studies of conformational unfolding of heterocyclic ureas)

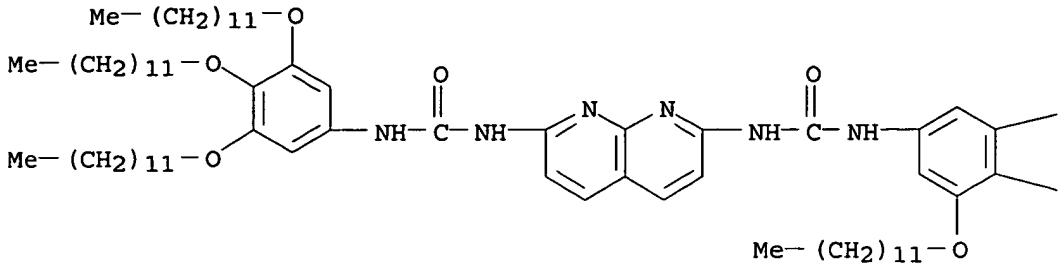
RN 380441-61-2 CAPLUS

CN Urea, N,N'-bis(5,7-dipropyl-1,8-naphthyridin-2-yl)-, compd. with N,N''-1,8-naphthyridine-2,7-diylbis[N'-[3,4,5-tris(dodecyloxy)phenyl]urea] (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 380441-54-3
CMF C94 H162 N6 O8

PAGE 1-A



PAGE 1-B

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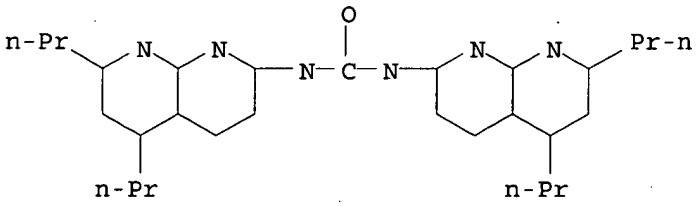
—O—$(CH_2)_{11}$—Me

CM 2

CRN 269063-80-1
CMF C29 H36 N6 O



*** FRAGMENT DIAGRAM IS INCOMPLETE ***
REFERENCE COUNT: 68 THERE ARE 68 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

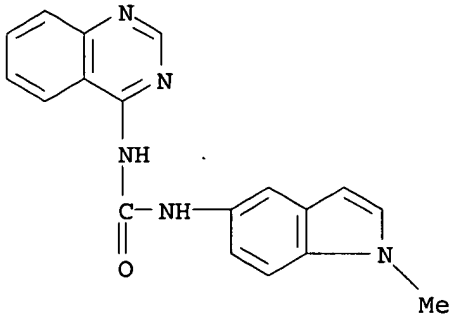
L3 ANSWER 12 OF 13 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:518623 CAPLUS
DOCUMENT NUMBER: 135:313150
TITLE: 1,3-Biarylureas as selective non-peptide antagonists of the orexin-1 receptor
AUTHOR(S): Porter, R. A.; Chan, W. N.; Coulton, S.; Johns, A.; Hadley, M. S.; Widdowson, K.; Jerman, J. C.; Brough, S. J.; Coldwell, M.; Smart, D.; Jewitt, F.; Jeffrey, P.; Austin, N.
CORPORATE SOURCE: New Frontiers Science Park North, GlaxoSmithKline Pharmaceuticals, Harlow, Essex, CM19 5AW, UK
SOURCE: Bioorganic & Medicinal Chemistry Letters (2001), 11(14), 1907-1910
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

10/ 019,945

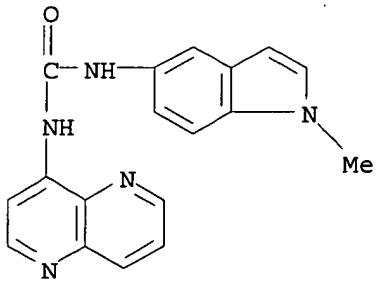
AB This communication reports SARs for the first orexin-1 receptor antagonist series of 1-aryl-3-quinolin-4-yl and 1-aryl-3-naphthyridin-4-yl ureas. One of these compds., 31 (SB-334867), has excellent selectivity for the orexin-1 receptor, blood-brain barrier permeability and shows in vivo activity following i.p. dosing.

IT **367953-08-0 367953-09-1 367953-12-6**
367953-13-7
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(1,3-Biarylureas as selective non-peptide antagonists of orexin-1 receptor)

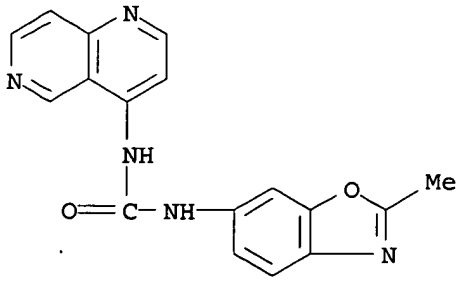
RN 367953-08-0 CAPLUS
CN Urea, N-(1-methyl-1H-indol-5-yl)-N'-4-quinazolinyl- (9CI) (CA INDEX NAME)



RN 367953-09-1 CAPLUS
CN Urea, N-(1-methyl-1H-indol-5-yl)-N'-1,5-naphthyridin-4-yl- (9CI) (CA INDEX NAME)



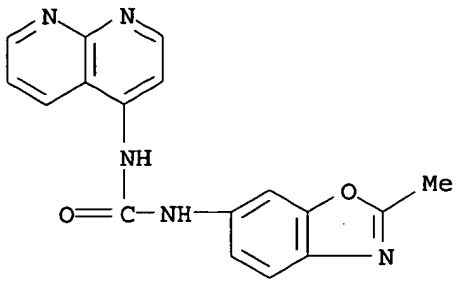
RN 367953-12-6 CAPLUS
CN Urea, N-(2-methyl-6-benzoxazolyl)-N'-1,6-naphthyridin-4-yl- (9CI) (CA INDEX NAME)



RN 367953-13-7 CAPLUS

10/ 019,945

CN Urea, N-(2-methyl-6-benzoxazolyl)-N'-1,8-naphthyridin-4-yl- (9CI) (CA INDEX NAME)

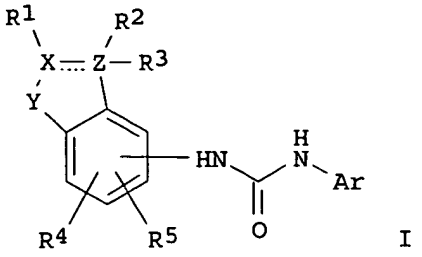


REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 13 OF 13 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:78363 CAPLUS
DOCUMENT NUMBER: 134:147614
TITLE: Preparation of N,N'-biarylurea derivatives as inhibitors of cyclin-dependent kinases (Cdk4 and Cdk6)
INVENTOR(S): Hayama, Takashi; Hayashi, Kyoko; Honma, Mitsutaka; Takahashi, Ikuko
PATENT ASSIGNEE(S): Banyu Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 460 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001007411	A1	20010201	WO 2000-JP4991	20000726
W: AE, AG, AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CR, CU, CZ, DM, DZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, KG, KR, KZ, LC, LK, LR, LT, LV, MA, MD, MG, MK, MN, MX, MZ, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
JP 2001106673	A2	20010417	JP 2000-274175	20000726
EP 1199306	A1	20020424	EP 2000-949909	20000726
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				

PRIORITY APPLN. INFO.: JP 1999-211384 A 19990726
WO 2000-JP4991 W 20000726
OTHER SOURCE(S): MARPAT 134:147614
GI



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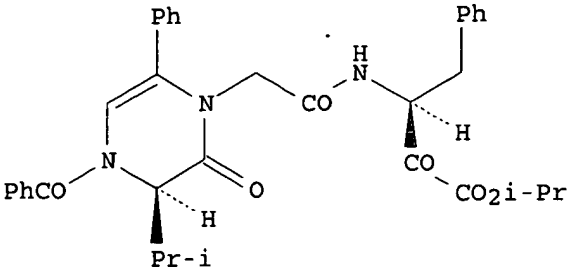


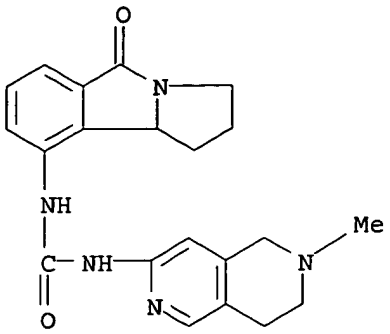
II

AB N-(hetero)aryl-N'-heterocyclylurea derivs. represented by general formula (I) [wherein Ar represents a nitrogenous heterocyclic arom. group such as (un)substituted pyridyl, pyrimidinyl, pyrazinyl, pyridazinyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, pyrazolyl, pyrrolyl, imidazolyl, indolyl, isoindolyl, quinolyl, isoquinolyl, benzothiazolyl, or benzoxazolyl; X and Z each represents C or N or together with R1 or R2 and/or R3 represent CH or N; Y represents CO, SO, or SO2; R1 represents hydrogen, (un)substituted lower alkyl, Y3-W2-Y4-R5, etc.; wherein R5 = H, (un)substituted lower alkyl, lower alkenyl, lower alkynyl, lower cycloalkyl, aryl, imidazolyl, isoxazolyl, isoquinolyl, isoindolyl, indazolyl, indolyl, indolidinyl, isothiazolyl, ethylenedioxyphenyl, oxazolyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, pyrazolyl, quinoxalinyl, quinolyl, etc.; W2 = ingle bond, O, S, SO, SO2, N-(un)substituted NH, SO2NH, NHSO2NH, NHSO2, CONH, NHCO, NHCONH, NHCO2, etc.; Y3, Y4 = single bond, linear or branched lower alkylene; R2 and R3 each represents hydrogen, lower alkyl or alkoxy, or Y3-W2-Y4-R5 (Y3, W2, Y4, R5 = same as above), or one of R2 and R3 together with R1 and X forms cyclohexane, cyclopentane, piperidine, 3,4,5,6-tetrahydro-1,3-oxazine, tetrahydrothiopyran, pyrrolidine, tetrahydrothiofuran, oxazolidine ring, etc.; R4 and R5 represent H, halo, OH, amino, or Y3-W2-Y4-R5 (Y3, W2, Y4, R5 = same as above)] or salts thereof are prepd. The compds. (e.g. II) have a remarkable proliferation-inhibitory effect on tumor cells. A Cdk4 and/or Cdk6 inhibitor for use in the therapy of malignant tumor can hence be provided. II showed IC50 of 0.061 and 0.019 .mu.M against cyclin-D1-Cdk4 and cyclin-D2-Cdk4, resp., vs. 0.36 and 0.056 .mu.M, resp., for (.+-.)-flavopiridol, and inhibited the proliferation of HCT116 and MKN-1 cells with IC50 of 0.013 and 0.10 .mu.M, resp., vs. 0.15 and 0.87 .mu.M, resp., for (.+-.)-flavopiridol. Pharmaceutical formulations contg. I were prepd.

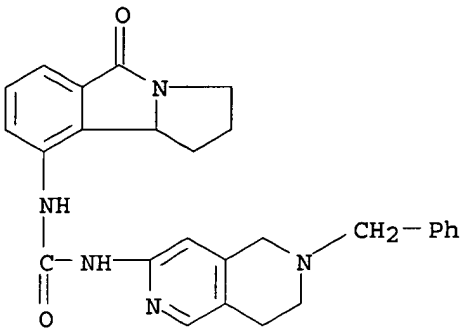
IT **322686-07-7P 322686-08-8P 322686-09-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of N-(hetero)aryl-N'-heterocyclylurea derivs. as inhibitors of cyclin-dependent kinases (Cdk4 and Cdk6) and antitumor agents)

RN 322686-07-7 CAPLUS

CN Urea, N-(5,6,7,8-tetrahydro-6-methyl-2,6-naphthyridin-3-yl)-N'-(2,3,5,9b-tetrahydro-5-oxo-1H-pyrrolo[2,1-a]isoindol-9-yl)- (9CI) (CA INDEX NAME)



RN 322686-08-8 CAPLUS
CN Urea, N-(2,3,5,9b-tetrahydro-5-oxo-1H-pyrrolo[2,1-a]isoindol-9-yl)-N'-[5,6,7,8-tetrahydro-6-(phenylmethyl)-2,6-naphthyridin-3-yl]- (9CI) (CA INDEX NAME)



RN 322686-09-9 CAPLUS
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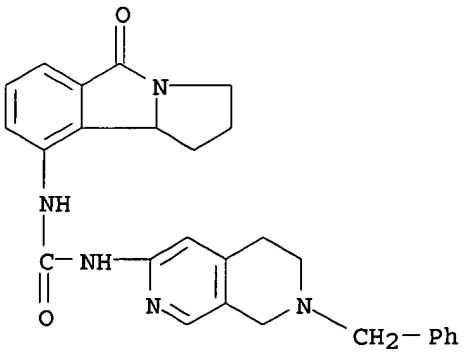

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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FILE 'REGISTRY' ENTERED AT 09:16:37 ON 03 DEC 2003
L1 STRUCTURE UPLOADED
L2 53 S L1 FUL

FILE 'CAPLUS' ENTERED AT 09:17:46 ON 03 DEC 2003
L3 13 S L2

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FULL ESTIMATED COST	59.80	208.56

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-8.46	-8.46

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